Out-of-office blood pressure monitoring in chronic kidney disease

Rajiv Agarwala, Aldo J. Peixotob, Sergio F.F. Santosc and Carmine Zoccald

Blood pressure (BP) control is vital to the management of patients with chronic kidney disease (CKD) yet most treatment decisions use BPs obtained in the clinic. The purpose of this report is to review the importance of self-measured and automatic ambulatory BPs in the management of patients with CKD. Compared with clinic-obtained BPs, self-measured BP more accurately defines hypertension in CKD. Masked hypertension seems to be associated with higher risk of end-stage renal disease in CKD patients. Conversely, white-coat hypertension seems to be associated with better renal outcomes than those who have persistent hypertension. Ambulatory BP monitoring is the only tool to monitor BP during sleep, diagnose nondipping, and, as self-measured BPs, have greater prognostic power in CKD compared with clinic BP. In hemodialysis patients, self-measured BP, but not pre/post-dialysis BP, shares the combination of high sensitivity and high specificity of greater than 80% to make a diagnosis of hypertension with the reference standard of ambulatory BP monitoring. In addition, self-measured and ambulatory BPs seem to be better correlates of left-ventricular hypertrophy and mortality in hemodialysis patients compared with pre/post-dialysis BP. Emerging data suggest that out-of-office BP monitoring is superior to BP obtained in the clinic when predicting target-organ damage and prognosis. Out-of-office BP monitoring is recommended for the management of hypertension in all stages of CKD. Blood Press Monit 14:2–11 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Introduction

The diagnosis and management of hypertension in patients with chronic kidney disease (CKD) rests, almost entirely, on blood pressure (BP) measurements obtained in a physician’s office where the mercury sphygmomanometer is rapidly being replaced by oscillometric devices [1]. It is well established that in people with untreated essential hypertension, a log-linear and continuous relationship exists between usual BP and stroke, ischemic heart disease, and other vascular mortality; with every 20 mmHg reduction in systolic BP and every 10 mmHg reduction in diastolic BP, vascular mortality is cut by half [2]. Like vascular disease, the incidence of end-stage renal disease (ESRD) is strongly linked to hypertension. In 332,544 men with hypertension who were screened for the Multiple Risk-Factor Intervention Trial, the relative risk of ESRD from any cause increased more than 20-fold from BP less than 120/80 to BP greater than 180/110 mmHg [3]. Current recommendations suggest targeting BP to less than 130/80 mmHg in patients with CKD, which is 10 mmHg lower than in those with essential hypertension [4]. These targets are based on BPs obtained in the physician offices.

There is now solid evidence that out-of-office recordings of BP in the general population can effectively refine risk stratification. Perloff et al. [5], in their pioneering study, demonstrated that ambulatory BP monitoring (ABPM) was superior to clinic BP in predicting cardiovascular events in patients with hypertension. The superior ability to risk stratify by ABPM has been confirmed in the general population [6–8], treated hypertensive patients [9], untreated hypertensive patients [10], refractory hypertension [11], and isolated systolic hypertension in the elderly [12]. As the management of hypertension is based on office-obtained BP, Kikuya et al. [13] have reported the ambulatory BP thresholds that yield 10-year cardiovascular risks similar to those associated with optimal (120/80 mmHg), normal (130/85 mmHg), and high (140/90 mmHg) BP on office measurement using 24-h ABPM data from 5682 participants (mean age 59.0 years; 43% women) enrolled in prospective population studies in Denmark, Belgium, Japan, and Sweden. Approximate thresholds for ‘optimal’ ambulatory BP after multivariate adjustment amounted to 115/75 mmHg for 24 h, 120/80 mmHg for daytime, and 100/65 mmHg for nighttime. Rounded thresholds for ‘normal’ ambulatory
BP were 125/75, 130/85, and 110/70 mmHg, respectively, and those for ambulatory ‘hypertension’ were 130/80, 140/85, and 120/70 mmHg.

Although the problem has been little investigated in patients with CKD, self-measured BP and ambulatory BP recordings may reduce misclassification of hypertension and increase our ability to predict renal and cardiovascular events in patients with CKD [14]. The purpose of this review is to discuss the use of out-of-office BP measurement techniques including self-measured BP and automatic ambulatory BP recordings in the management of patients with CKD. We will discuss the value of these methods separately for patients with CKD not on dialysis and those on dialysis. Patients who have received a kidney transplant are not the subject of this review.

**Chronic kidney disease not on dialysis**

**Out-of-office blood pressure monitoring and blood pressure profile**

Despite the recognition that hypertension is a strong, modifiable, and continuous risk factor for renal and cardiovascular outcomes in CKD, measurement of BP is often not performed using standardized methods. White-coat hypertension is widely accepted as a clinical entity, even though the reproducibility of the white-coat effect is still undetermined. Masked hypertension – elevated BP at home, but normal BP in the clinic – still remains a scarcely characterized entity in the general as well as in the hypertensive population [15]. A recent systematic review estimated that the prevalence of this condition is between 8 and 20% in the general population and to be as high as 50% among treated hypertensive patients [16].

When standardized methods of measurements are used, the prevalence of white-coat hypertension in mostly male veterans with CKD is found to be at least as high (approximately 30%) as that found in the general population [17]. The overall prevalence of masked hypertension was in 26–29% by clinic BP, but only 13% with home BP monitoring [17] In a large Italian study of 290 patients with CKD, the prevalence of white-coat hypertension was 31.7% and those with white-coat hypertension were less likely to have proteinuria and left-ventricular hypertrophy [18]; masked hypertension was present in 5.9% of the patients [18]. In patients with diabetes mellitus and albuminuria, the prevalence of white-coat hypertension is reported to be 9% [19] and in children with CKD the prevalence is quite high at 23% [20].

Despite more aggressive BP targets, hypertension control rates in patients with CKD are poor both in the United States [21–23] and in the Europe [24]. Only 37% of people with CKD have BP less than 130/80 mmHg. People who have worse BP control are more often black, older, and have albuminuria [22]. Poor control rates mostly center about elevated systolic BP in people who are more often obese, black, or male [23]. In addition, poor control can be attributed to high prevalence of white-coat hypertension in those with CKD.

Home BP monitoring improves the diagnosis of hypertension. When compared with the reference standard of ABPM in patients with CKD, home BP monitoring has the best diagnostic performance compared with routine or standardized clinic measurements [17]. Receiver-operating characteristic analysis of diagnostic test performance shows a higher area under the curve compared with clinic BP. One week-averaged home BP of greater than 140/80 mmHg is associated with awake ambulatory BP of greater than 130/80 mmHg, which is considered hypertensive in patients in the CKD population. These thresholds of systolic and diastolic BPs have a sensitivity of greater than 80% and specificity of greater than 80%; accordingly, these thresholds may be useful for clinical decision-making.

Systemic arterial pressure shows a distinct arterial rhythm that is related to the sleep–awake cycle and only ambulatory BP recordings – not office BP or self-measured BP – can reveal such variations. Patients who have less than 10% decline in night BP compared with day BP are called ‘nondippers’ [25] and in the general population patients with nondipping have been shown to have an elevated risk of cardiovascular events independent of the BP load [26]. Nondippers and those with 24-h pulse pressure of greater than 53 mmHg [27] are considered at high risk for cardiovascular events [28]. ABPM in patients with CKD has led to the identification of loss of nocturnal decline in BP [29,30]. Although the exact mechanism of nondipping remains elusive, volume excess [31], autonomic dysfunction [29], sympathetic activation [32], sleep apnea [33], physical activity [34], and low glomerular filtration rate (GFR) [35,36] are proposed.

Nocturnal hypertension is a stronger predictor of cardiovascular outcomes than daytime hypertension perhaps, because these measurements are better standardized as most patients are resting or sleeping during this time [10]. During the day, physical activity, emotional stress, and environmental factors are stressors of BP and may provide an index of hemodynamic reactivity. Although these data suggest that daytime ABPM better predicts ESRD and nighttime ABPM predicts cardiovascular events, these results need to be confirmed in future studies. If replicated, it would suggest that the BP level during the day and night might have differential prognostic information.

Physical activity-induced increase in BP is related to cardiovascular events [37–41]. In a study by Agarwal and Light [42], 24 patients with CKD had 24-h ABPM and
simultaneous activity monitoring with wrist actigraphy. Nondippers have a greater level of sleep activity compared with dippers, although the awake activity level was similar between groups. Patients who are more sedentary had a greater increment in systolic BP with physical activity compared with those who are less sedentary. Antihypertensive drugs blunted hemodynamic reactivity. Hemodynamic reactivity was greatest between 00:00 and 08:00 h making this a vulnerable period for cardiovascular events. Thus, interventions to reduce BP reactivity may be clinically useful. For example, regular exercise may blunt hemodynamic reactivity as can antihypertensive drugs. As BP variation is associated with increased cardiovascular damage, attenuation of hemodynamic reactivity with antihypertensive drugs may be an additional mechanism of cardiovascular protection.

Out-of-office blood pressure and target-organ damage
Many patients with CKD die of cardiovascular causes, whereas others progress to ESRD [43]. In type 1 diabetic patients, a 5 mmHg rise in nighttime systolic BP resulted in a 44% increased risk of development of microalbuminuria that office BP was unable to detect [44]. In addition, among patients with type 1 diabetes mellitus, nighttime BP was directly correlated with structural lesions in kidney biopsies [45,46]. In a cross-sectional analysis, Agarwal and Andersen [55] observed that proteinuria was the strongest correlate of systolic BP measured by any technique – routine or standardized office, home or 24-h ABPM. The relationship was weakest for routine, stronger for standardized, and the best for home and ambulatory BPs. Other small cross-sectional studies show a stronger relationship of ABPM with left-ventricular hypertrophy in children with CKD [47], in normotensive patients with autosomal-dominant polycystic kidney disease [48] and adults with CKD but without diabetes mellitus or vascular disease [49]. Finally, in the African American Study of Kidney Disease, greater average nighttime and daytime systolic ABPM, lower estimated GFR (eGFR), and younger age (but not proteinuria or hematocrit) were independent correlates of echocardiographic left-ventricular hypertrophy [50]. Taken together, these data support the hypothesis that out-of-office BP monitoring may be associated with better cardiorenal-risk stratification when compared with office measured BPs.

Out-of-office blood pressure and prognosis
Misclassification of hypertension diminishes the prognostic implication of high BP in the general population [51]. Rave et al. [52] studied 77 patients with type 1 diabetic nephropathy and reported that after a mean follow-up of approximately 6 years, self-measured BP was a stronger predictor of decline in GFR compared with office BP. Agarwal and Andersen [53] compared the prognostic value of clinic and home BP monitoring (three measurements/day for one week) in a cohort of 217 mostly male veterans with CKD. In this study, home BP was prognostically superior to clinic BP and predicted ESRD independently of proteinuria, eGFR, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker use, and other risk factors. In this study, masked hypertension entailed an increased risk of ESRD, whereas the risk associated with white-coat hypertension was much lower compared with that of sustained hypertension (Fig. 1).

When compared with clinic BP, ABPM was superior in predicting the composite endpoint of death or ESRD [53]. Daytime BP was a stronger predictor of ESRD compared with nighttime BP. Although nondipping was associated with worse outcomes, it was not of independent value when other adjustments were made. ABPM did not improve the predictive value of home BPs. When cardiovascular outcomes were analyzed in this cohort, nondipping was associated with increased cardiovascular risk, but not when adjusted for other risk factors using propensity scores [54]. Thus, it seems that risk factors such as poor renal function that leads to non-dipping may also increase cardiovascular risk in patients with CKD.

In contrast to the above reports, Davidson et al. [55] have reported that nondipping was a risk factor for subsequent decline in eGFR. Baseline level of eGFR was 80.5 ml/min/1.73 m² in dippers and 76.4 ml/min/1.73 m² in nondippers, and levels at follow-up were 81.0 and 64.7 ml/min/1.73 m², respectively. Given the well-preserved eGFR at baseline and lack of information on albuminuria – the most important risk factor for future decline in GFR – the extrapolation of these findings to patients with CKD should be very cautious. Several small studies have shown worse renal outcomes in patients with nondipping, such as a more rapid decline in renal function in patients with hypertension and CKD [56], those with diabetic nephropathy [57], and among normotensive patients with immunoglobulin A nephropathy [58]. Reproducibility of dipping in patients with CKD has been scarcely studied. Available data suggest that the reproducibility of this phenomenon is unsatisfactory in these patients [59]. Further research is needed to better determine the clinical and prognostic value of nondipping in CKD.

The translation of this groundwork in ABPM to the treatment setting has not yet been made. Early attempts have attempted converting nondippers to dippers by administering antihypertensive drugs in the evening [60,61]. In an 8-week prospective, uncontrolled study, Minutolo et al. [60] studied 32 patients with GFR less than 90 ml/min/1.73 m². All patients were nondippers (night/day BP ratio > 0.9), and all had acceptable daytime BP levels (< 135/85 mmHg). The intervention was a change in the time of dosing of one of the antihypertensive agents that the patient was receiving.
from the morning to the evening. The authors observed a decrease in the night/day ratio in 94% of the patients, and that an arbitrary dipper status (night/day ratio < 0.9) was attained in 88% of the patients. These changes were achieved without a deleterious impact on daytime BP, and were associated with a modest reduction in 24-h protein excretion. Although pilot in nature, these results underscore the prospects of valuable modulation of the circadian BP rhythm in CKD. It remains to be seen whether modulation of circadian BP rhythms would have an independent effect on hard outcomes.

**Hemodialysis patients**

Mansoor and White [62] in a review published in 1997 stated that ‘the available data on BP control in dialysis patients indicated that current methods of monitoring hypertension are suboptimal. However, these patients show marked BP variability, and studies are necessary to determine the best ways to monitor and manage hypertension’. Substantial progress has been made over the last decade in BP monitoring techniques in patients on dialysis.

**Out-of-office blood pressure monitoring and blood pressure profile**

When peridialysis BPs are used to predict total mortality, a reverse relationship between BP and total mortality is seen [63]. This may be because of reverse causation or poor assessment of BP in the hemodialysis population [64]. The latter is supported by the observation that
although nearly 60% of pediatric hemodialysis patients [65] and 80% of adult hemodialysis patients are found to be hypertensive, 30% with good control, using routine BP measurements [66], only 33% are hypertensive patients in an unselected population using 44-h interdialytic ABPM [67]. Thus, white-coat effect or measurement errors must account for a large percent of seemingly uncontrolled hypertensive patients among hemodialysis patients. ABPM is an important tool to clarify the mean level of BP, nocturnal hypertension, and the dipping phenomenon [68]. Information on the reproducibility of dipping in hemodialysis patients is still limited [69,70]. A categorical analysis by Peixoto et al. [68,69] in 21 patients showed that 43% of patients changed dipping status on retesting. An analysis based on the classical Altman–Bland plot by Tripepi et al. [70] in 19 patients showed that in no patient the day–night difference exceeded 2 standard deviation, with 14 patients (74%) displaying a difference ≤ 0.1, indicating fairly good reproducibility. Discrepancy between the two studies may be attributable to the methodological approach (categorical vs. continuous analyses), as well as on the composition of the cohorts. Further, these studies emphasize the need for more research in this area.

Peridialysis BPs that are routinely obtained in the dialysis unit before and after dialysis without using a specified technique may be useful in a qualitative sense but cannot be used to determine interdialytic BP [71]. For example, among 70 patients on chronic hemodialysis, who underwent ABPM for the diagnosis of hypertension, Agarwal et al. [72] found that the agreement limits between pre/post-dialysis BP and ambulatory BP are sufficiently wide to preclude determination of ambulatory BP. Predialysis BP of greater than 150/85 mmHg has greater than 80% sensitivity but is not sufficiently specific in diagnosing hypertension. Postdialysis BP of greater than 130/75 mmHg also has greater than 80% sensitivity but is not sufficiently specific in diagnosing hypertension when the reference standard of ABPM is used. Similar results were obtained in a meta-analysis, which found poor agreement between ambulatory BP recordings and pre/post-dialysis BP measurements [73].

However, intradialytic BPs may be useful to diagnose hypertension. Agarwal et al. [74] reported median intradialytic cut-off systolic BP of 140 mmHg from a single dialysis provided approximately 80% sensitivity and 80% specificity in diagnosing systolic hypertension; a median cut-off diastolic BP of 80 mmHg provides approximately 75% sensitivity and 75% specificity in diagnosing diastolic hypertension with the reference standard of interdialytic ABPM. Thus, consideration of intradialytic BPs together with predialysis and postdialysis BPs seems to improve the reproducibility, accuracy, and precision of BP measurement. In addition, the use of the intradialytic median adds an element of practicality to the analysis, as clinicians may be able to estimate it much more easily than performing a bedside calculation of the intradialytic mean.

In an unselected population of hemodialysis 150 patients, Agarwal et al. [75] performed interdialytic 44-h ABPM, home BP monitoring three times daily for 1 week, predialysis and postdialysis BP measurement using routine and standardized techniques. Only about one in three patients was hypertensive, defined as awake ambulatory BP of 135/85 mmHg or more. There was poor agreement between ambulatory and peridialysis BPs; better agreement was seen between home and ambulatory BPs. The area under the receiver-operating characteristic curve was greatest for home BP. Home BP of 150/80 mmHg or more had at least 80% sensitivity and 80% specificity in diagnosing hypertension.

On account of uncertainties in the evaluation of BP, it is unclear whether hemodialysis patients who are being treated with medications are truly hypertensive. Home BP monitoring can also be useful to decide when a hemodialysis patient does not need antihypertensive drugs. To ascertain the appropriateness of antihypertensive therapy, Bishu et al. [67] conducted a prospective study in which they discontinued antihypertensive drugs in hemodialysis patients and performed 44-h interdialytic ABPM and measured left-ventricular mass and inferior vena cava by echocardiography. Home BP was monitored weekly during washout. An average of 2.3 medications were tapered and discontinued in 41 Black participants (age 56 years, 46% men, 54% diabetes mellitus, duration of dialysis 5.3 years). Thirty-three of 41 (80%) patients became hypertensive but eight (20%) remained normotensive at 3–5 weeks. Those patients who remained normotensive had lower home BP at baseline (135/76 vs. 147/85 mmHg) and had a lower left-ventricular mass index (115 vs. 146 g/m2). The rate of rise of home BP was more rapid in those patients who became hypertensive. None of the normotensive patients were volume overloaded in contrast to 12% of the hypertensive patients. Thus, patients with well-controlled home BP who have no left-ventricular hypertrophy may have a cautious withdrawal of their antihypertensive drugs.

In a randomized trial of 44 Canadian hemodialysis patients, Deziel et al. [76] evaluated the utility of automatic adjustment of ultrafiltration and dialysate conductivity, and used self-measured BP monitoring to detect improvement in hypertension. In doing so, these authors demonstrated for the first time the usefulness of self-measured BP to detect BP responses to interventions in hemodialysis patients in a randomized controlled trial setting [76].

Emerging data suggest that the minimum duration for adequate self-measured BP recordings in hemodialysis
should include at least twice daily BP after the mid-week dialysis for 4 days [77]. Alternatively, BP obtained thrice daily for 1 week can be used.

Interpreting ABPM recording is typically performed by averaging a large number of BP measurements, which gives a better reflection of patient’s true BP. The lack of fall in BP during sleep can be calculated by averaging BP during the day and during the night, but such a reductionist approach obscures the rhythmic changes in BP over a 24-h period [78–80]. To study this blunting in circadian variation, modeling BP using cosinor rhythmometry has been proposed [81]. The amplitude, periodicity, and time to peak and trough can all be analyzed using this technique. The application of this model in patients with ESRD has yielded valuable insights [82].

In the renoprival state, gain of volume over an interdialytic period leads to increase in BP. The traditional cosinor model requires ‘midline estimating statistic of rhythm’, defined as the average value of the rhythmic function fitted to the data to be flat [81]. Gain in volume over an interdialytic interval may cause a steady increase in systemic arterial pressure between two dialysis treatments and the above assumption of a flat midline estimating statistic of rhythm may no longer be tenable. Thus, a more complex model that includes terms for cosinor as well as a straight line change would be more appropriate to describe the data (Fig. 2). Kelley et al. [83] have developed a trended cosinor model that includes both parameters – one for linear trend and another for the cosinor. Using this model, the authors demonstrated that antihypertensive drug therapy blunts the interdialytic linear trend but has a U-shaped relationship to the amplitude of systolic and diastolic BP patterns in the interdialytic interval.

**Out-of-office blood pressure and target-organ damage**

One way to assess the value of BP obtained by various techniques as a marker of risk is to correlate it with left-ventricular hypertrophy, a potent correlate of cardiovascular outcomes in hemodialysis patients. Predialysis BP as well as 24-h ABPM was associated with echocardiographic left-ventricular mass index in a series of 64 nondiabetic hemodialysis patients without heart failure [84]. Small, albeit significant correlations were seen with 44-h interdialytic ABPM ($r^2=0.06$) and 1 week-averaged home BP ($r^2=0.09$). Similarly, Rahman et al. [79] demonstrated the relationship of nondipping with left-ventricular mass index in a cross-sectional study, and a Japanese study using averaged BPs over 1 week obtained within and outside the dialysis unit showed significant positive correlations with the left-ventricular mass index ($r=0.387$, $P < 0.001$) and brachial artery pulse wave velocity ($r=0.226$, $P < 0.05$) in contrast to predialysis systolic BP [85].

Besides an overall increase in BP, hemodialysis patients have marked disturbances in interdialytic ABPM pattern that is characterized by blunted circadian amplitude and a steady rise in BP between dialysis treatments as discussed above. The pathophysiology of this abnormal BP profile was explored in a cross-sectional study by Agarwal and Light [86]. They hypothesized that the circadian amplitude, the interdialytic increase (linear trend), and the average level of BP (the intercept) are related to the extent of arterial stiffening and the degree of accumulation of salt and water between dialysis. Using a generalized cosinor model, they simultaneously compared the impact of interdialytic weight gain and echo-Doppler-measured aortic pulse wave velocity on the mean level of BP, linear changes over the interdialytic interval, and oscillatory changes in BP. They reported that aortic pulse wave velocity and interdialytic weight gain had a substantial impact on interdialytic ambulatory BP level, linear trends and rhythms. Although arterial stiffness was associated with an overall increase in the level (intercept) of systolic, diastolic, and pulse pressures, interdialytic weight gain, in contrast, was associated with interdialytic increase (linear trend) in BP. The circadian amplitude was blunted by increments in either arterial stiffness or interdialytic weight gain [86].

**Out-of-office blood pressure and prognosis**

A few studies have assessed the prognostic power of ABPM and outcomes in hemodialysis patients. Amar et al. [87] followed 57 hypertensive hemodialysis patients in France for about 3 years and demonstrated that nocturnal systolic BP and 24-h pulse pressure were independent risk factors for cardiovascular deaths. Liu et al. [88]
reported that among 89 Japanese hemodialysis patients, the incidence of cardiovascular events and deaths were 3.5–9 times higher in nondippers compared with dippers. 

Tripepi et al. [70] in a much larger study of 168 Italian hemodialysis patients without diabetes mellitus found that the ratio of night/day systolic BP was associated with all-cause mortality and cardiovascular mortality in multivariable Cox models. More recently, Alborzi et al. [89] reported a cohort of 150 U.S. patients who had initial assessment of peridialysis BP, home BP, and ABPM to assess the relationship of BP with all-cause mortality and cardiovascular mortality. One standard deviation increase in systolic BP increased the risk of death by 1.46 (95% confidence interval: 1.09–1.94) for ambulatory, 1.35 (95% confidence interval: 0.99–1.84) for home, and between 0.97 and 1.19 (P > 0.20) for dialysis unit BP recording. Figure 3 shows the relationship between quartiles of systolic BP obtained by various methods and the hazard ratio for all-cause mortality. Two points are notable. First, the second quartile was associated with a better survival compared with others. Second, trend for mortality was only statistically significant for home and ambulatory systolic BPs. Thus, in patients on hemodialysis, BPs obtained at home or by ABPM are stronger predictors of mortality than BPs obtained in the dialysis unit. Home BP ³ 150 mmHg confers mortality risk and average interdialytic BP of ³ 135 mmHg confers cardiovascular mortality and all-cause mortality risk. Further analysis indicates that among patients on hemodialysis, the location, not the quantity of BP recordings, obtained outside the dialysis unit seems to be associated with target-organ damage and mortality [77]. Finally, a Japanese study showed that pulse pressure derived from BPs obtained within and outside the dialysis unit when averaged over 1 week were predictive of cardiovascular mortality and all-cause mortality [90].

**Peritoneal dialysis patients**

**Out-of-office blood pressure profile**

The available data on out-of-office BP in peritoneal dialysis (PD) are much less contributory than in hemodialysis. In a large observational study of Italian PD patients, Cocchi et al. [91] performed 24-h ABPM in 414 patients, most of which received standard continuous ambulatory PD. The prevalence of hypertension was 88% based on office BP ³ 140/90 mmHg, and 69% based on BP load greater than 30%. These data suggest that the prevalence of hypertension is similar in PD as it is among large groups of hemodialysis patients. The additive diagnostic value of ABPM was addressed in a small study of 25 pediatric PD patients using the 95th percentile thresholds to define hypertension based on office and ambulatory BPs [92]. The prevalence of hypertension increased from 32% with clinic BP readings to 56% based on daytime ambulatory BP. Furthermore, elevated nocturnal BP values were observed in approximately two out of three patients [92]. In a study of 32 PD patients, Wang et al. [93] evaluated the relationship between home BP and 24-h BP. Home BP was taken as the 10-day average of three BP readings obtained in the morning using the auscultatory method. Bivariate analyses indicated high correlation coefficients between home BP and 24-h
BP values \( r = 0.54-0.71 \), although similar coefficients were obtained between clinic BP and 24-h BP. The impact of home BP on diagnosis or on target-organ damage was not addressed. However, the overall trend of these data suggests that there may be added value to the diagnosis of hypertension in PD by using out-of-office BP values.

The Italian database of Cocchi et al. [91] was also important, in that it provided the largest data set to interpret the circadian BP behavior in PD. In that respect, the frequency of nondipping was reported as 53%, and the mean difference between day and night BP was 8.7/5.7 mmHg. Other published series have produced variable results, but were of much smaller sample size [78,82,93–97]. In addition, different PD modalities (conventional ambulatory, cycler-assisted) seem to have similar diurnal BP profiles [91,93]. Finally, peritoneal membrane transport characteristics based on a conventional peritoneal equilibration test seem to be associated with overall BP levels (highest BP among high and high-average transport patients), but bear no relationship with dipping profile [98].

**Out-of-office blood pressure and target-organ damage**

Only left-ventricular hypertrophy and carotid artery distensibility have been studied in the realm of target-organ damage in PD, and it is not entirely clear that ambulatory BP holds stronger associations than office BP. Konings et al. [99] studied 41 PD patients with careful measures of volume status (bromide and deuterium spaces), carotid artery ultrasound, and echocardiography. Left-ventricular mass was positively associated with ambulatory BP values \( r=0.43 \) for systolic BP and 0.46 for diastolic BP), whereas office BP values did not hold a significant correlation. Wang et al. [93] reported that PD patients with echocardiographic evidence of left-ventricular hypertrophy (left-ventricular mass index \( > 125 \) g/m\(^2\) in men and \( > 100 \) g/m\(^2\) in women) had higher nocturnal BP than those without left-ventricular hypertrophy, and that nighttime systolic BP load greater than 30% was the only factor independently associated with the presence of LVH on multivariable analysis that adjusted for several relevant clinical, biochemical, and hemodynamic factors. However, they did not report on the associations between office BP or home BP and left-ventricular hypertrophy; thus, we cannot fully assess the additive effect of ABPM in this cohort. Tonbul et al. [95] further analyzed the association of nocturnal hypertension and left-ventricular hypertrophy in 24 PD patients, 88% of which were dippers, and 22 hemodialysis patients (18% dippers). Nondipping was associated with increased left-ventricular mass index when both PD and hemodialysis patients were taken together. Individual analyses did not reach statistical significance despite a consistent trend of higher left-ventricular mass index among nondippers in both groups \((155 \pm 40 \text{ vs. } 121 \pm 29 \text{ g/m}^2\text{ for hemodialysis, } 143 \pm 48 \text{ vs. } 133 \pm 30 \text{ g/m}^2\text{ for PD, and } 153 \pm 40 \text{ g/m}^2\text{ vs. } 131 \pm 29 \text{ g/m}^2\text{ for the entire group}) [95]. Unfortunately, the authors did not perform continuous analyses that take into account the degree of change in nighttime BP. In contrast, Ozcakar et al. [92] found similar correlations between left-ventricular mass index and office and ambulatory BP values, and were unable to show a relationship between dipping (quantitatively measured) and left-ventricular mass index in pediatric PD patients.

The sparse amount of data in patients on PD calls for larger studies to understand the impact of out-of-office BP on the diagnosis and prognosis of hypertension in this group. In view of the ambulatory nature of the PD process, we believe that the use of home BP needs to be a major focus of future research in the field.

**Conclusion**

BP recordings obtained without using standardized methods have substantial clinical implications. Opportunity exists for improvement in this single measurement in physician offices and hospitals. Emerging data support the notion that self-measured BP monitoring is indispensable to the management of hypertension in patients with CKD whether they are receiving dialysis or not. The strong predictive value of home BP in predicting ESRD outcomes even when adjusted for clinic BP, obtained using standardized methods, is evidence of home hypertension being an independent risk factor in CKD.

In hemodialysis patients, home BP of 150/80 mmHg or more has a combined sensitivity and specificity of greater than 80% in diagnosing hypertension defined by 24-h ABPM, making it an excellent tool for management of hypertension in the dialysis unit. Prospective randomized clinical trials are needed to show whether treatment guided by home BP values can influence cardio renal outcomes in patients with CKD.

Ambulatory BP recordings are the only practical way of making a diagnosis of nocturnal hypertension. Whether nondipping has independent value in predicting hard outcomes and, more importantly, whether restoration of dipping impacts cardio renal outcomes in patients with CKD remain to be demonstrated.

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**References**


72 Agarwal R, Lewis RR. Prediction of hypertension in chronic hemodialysis patients.

67 Bishu K, Gricz KM, Chewaka S, Agarwal R. Appropriateness of antihypertensive drug therapy in hemodialysis patients.


